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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,156	11/03/2003	Nathan Andrew Shapira	UF-389	3799

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EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
08/21/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/700,156	SHAPIRA ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed June 4, 2008 have been received and entered into the application. Upon further consideration, the restriction requirement mailed on April 4, 2008 have been withdrawn. Accordingly, claims 1-54 are being examined to the extent of Applicant's elected species, atomoxetine, on April 16, 2008.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 2, 10, 17 and 25 are rejected under 35 U.S.C. 102(a) as being anticipated by Michelson et al. (2003).

Michelson et al. teach that atomoxetine is effective for treatment of attention-deficit/hyperactivity disorder (ADHD). (abstract, conclusion). Michelson et al. teach that ADHD is a psychiatric disorder characterized by difficulties sustaining attention and difficulties with impulse control. (first sentence under Introduction). Michelson et al. teach that atomoxetine was administered 60mg of daily dosage and increased to 90 mg/day and to 120mg/day.

It is noted that in the instant specification on page 6, lines 10-15, that cognitive dysfunction is defined as a condition of having **difficulty with attention**. Therefore, the teaching of Michelson et al. that atomoxetine provided an efficacious treatment of ADHD characterized by difficulties sustaining attention clearly anticipates the claimed invention.

It is further noted that instant claims are drawn to **"an individual"**; therefore, the instant claims are clearly anticipated by Michelson et al's methodology involving the administration of the same active agent to the same subject population of any individual. Therefore any treatment or amelioration of medication induced cognitive dysfunction would be inherent of cited reference as well as applicants' any situations or disorders that are associated with cognitive disorders such as perioperative or stressful situation.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bymaster et al. (WO 03/049724 A1)(WO) and Bymaster et al. (2002) of record in view of Maki-Ikola (U.S.Patent No. 6,335,371B1) and further in view of Swaguchi et al. (1991) and Il'yuchenok (1988).

Bymaster et al. (WO) teach that atomoxetine is useful for the treatment of cognitive failure, including cognitive failure due to dementia, delirium and schizophrenia. (page 2, lines 21-30, page 3, line33- page 4, page 15, line 14-20). Bymaster et al.

teach that the treatment of cognitive failure refers to cognitive dysfunctions ranging from mild cognitive impairment to deterioration of intellectual function and other skills severe enough to interfere with the ability to perform activities of daily living; and dementia related to other medical conditions. (page 3, lines 3-9, pages 18 and 19).

Bymaster et al. (2002) teach that atomoxetine increases catecholamine in prefrontal cortex (PFC), a region involved in attention and memory in ADHD. Bymaster et al. teach that atomoxetine increase dopamine concentration in PFC 3-fold, but does not alter dopamine in stratum. This is in contrast to methylphenidate increasing catecholamine in PFC, suggesting it would not have drug abuse liabilities. (abstract).

Bymaster et als' do not teach the treatment of specific population to be treated including populations with medication-induced cognitive dysfunction set forth in claims 1, 31, perioperative cognitive dysfunction set forth in claims 4, 5, 34 and cognitive dysfunction that is associated with a stressful situation set forth in claim 38; the specific medications set forth in claim 54; employment to an individual with the normal range of cognitive function set forth in claims 10-12,and the employment of bupropion.

Maki-Ikola teaches that cognitive impairment is often related to the usage of drugs, such as benzodiazepines and tricyclic antidepressants, which are common in the treatment of different somatic diseases and psychiatric disorders. Maki-Ikola teaches that cognitive impairment is also related to post traumatic stress disorder. (column 2, lines 5-20).

Kellinger et al. teaches that cognitive disorders may be caused by brain injury result from trauma, alcoholism, drug dependency, stroke and severe head wounds. (column 1, lines 10-20).

Swaguchi et al. teach that the prefrontal cortex is involved in the cognitive process of working memory. (abstract). Swaguchi et al. teach that the activation of dopamine receptors is critical for the memory processes mediated by the primate PFC. (page 949, last paragraph).

Il'yuchenok teaches that bupropion, a selective blocker of the reverse uptake of dopamine, prevented development of amnesia. Il'yuchenok teaches that bupropion also facilitates retrieval of memory traces affected by amnesia or spontaneous or induced forgetfulness. (abstract).

It would have been obvious to one of ordinary skill in the art to employ atomoxetine for the treatment of cognitive dysfunction caused by or associated with medication (e.g. anti-depressant medication, anti-anxiety medications or diazepam). perioperative conditions (e.g. incomplete or heavy pain control, craniectomy) and stressful conditions because atomoxetine is useful for the treatment of cognitive dysfunction as taught by Bymaster et al's in general referring to cognitive dysfunctions ranging from mild cognitive impairment to deterioration of intellectual function and other skills severe enough to interfere with the ability to perform activities of daily living in general, and because the usage of drugs or medications, such as benzodiazepines (diazepam, antianxiety medication) and tricyclic antidepressants causes cognitive dysfunctions and affects intellectual functions as taught by Maki-Ikola. Further,

Kellinger et al. teaches that cognitive disorders are caused or associated with brain injury due to trauma, stroke and severe head wounds which are involved with perioperative conditions associated with degree of pain control and these conditions would also encompassed by teaching of treatment of cognitive dysfunctions which interfere with the ability to perform activities of daily living taught by Bymaster et al.

It would have been obvious to one of ordinary skill in the art to employ atomoxetine for optimizing cognitive function in individuals when untreated, is in normal range because atomoxetine increases dopamine concentration in PFC as taught by Bymaster et al.(2002) and this increase of dopamine concentration is critical for the memory process in primates as taught by Swaguchi et al. One would have been motivated to employ atomoxeine for the optimization of cognitive dysfunction in an individual including students, athletes etc. in order to achieve an expected benefit of increase in attention and memory in a subject by increasing critical catecholamine concentration in PFC that is critical for obtaining the memory processes. There is a reasonable expectation of success in optimizing cognitive function for individuals with normal cognitive function because atomoxetine possess chemical/physical characteristics of increasing critical catecholamine concentration if PFC critical for memory processing.

Further, it would have been obvious to one of ordinary skill in the art to combine bupropion for the treatment of cognitive dysfunction or optimizing cognitive function in normal individual because bupropion facilitates retrieval of memory traces affected by amnesia or spontaneous or induced forgetfulness as taught by Il'yuchenok. One would

have been motivated to combine bupropion with atomoxetine in order to achieve at least an additive effect in improving cognitive dysfunction/function. The motivation for combining the components flows from their individually known common utility (see In re Kerkhoven, 205 USPQ 1069(CCPPA 1980)). The amounts of active agents to be used for the daily treatment, the pharmaceutical forms, e.g., tablets, etc; mode of administration, flavors, surfactant are all deemed obvious since they are all within the knowledge of the skilled pharmacologist and represent conventional formulations and modes of administration. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

None of the claims are allowed.

Response to Arguments

Applicants' arguments filed January 10, 2007 have been fully considered but they are not persuasive. Applicants argue that with regard to the previous 102 rejection anticipate by Michelson et al. (2003), that it fails to teach 1) the treatment of amelioration of medicament-induced cognitive dysfunction; 2) the treatment or amelioration of perioperative cognitive dysfunction; 3) the treatment or amelioration of cognitive dysfunction associated with, or arising from, a stressful situation; or 4) the optimization of cognitive dysfunction in individual whose cognitive function tests in the

normal range. This is not found to be persuasive because the instant claims are drawn to "an individual" which reads on any subject population. Michelson et al's methodology involving the administration of the same active agent to the same subject population of any individual is the same as the single method steps recited the instant claims. Therefore any treatment or amelioration of medication induced cognitive dysfunction would be inherent of cited reference as well as applicants' any situations or disorders that are associated with cognitive disorders such as perioperative or stressful situation. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Kim/
Primary Examiner, Art Unit 1617

Jmk
August 18, 2008